General

Guideline Title

Lipids and lipoproteins. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents.

Bibliographic Source(s)

Lipids and lipoproteins. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. p. 184-281. [158 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions of the levels of the evidence (A, B, C, D) and strength of recommendations are presented at the end of the "Major Recommendations" field.

Note from the National Heart, Lung and Blood Institute (NHLBI) and the National Guideline Clearinghouse (NGC): Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents has been divided into individual summaries covering the major cardiovascular risk factors. In addition to the current summary, the following are available:

- Family history of early atherosclerotic cardiovascular disease
- Nutrition and diet
- Physical activity
- Tobacco exposure
- High blood pressure
- Overweight and obesity
- Diabetes mellitus and other conditions predisposing to the development of accelerated atherosclerosis
- Risk factor clustering and the metabolic syndrome
- Perinatal factors

Recommended Cut Points for Lipid and Lipoprotein Levels (mg/dL) in Young Adults*

NOTE: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Category	Acceptable	Borderline High	High
TC	<190	190-224	≥225
LDL–C	<120	120–159	≥160
HDL–C	<150	150–189	≥190
TG	<115	115–149	≥150

Category	Acceptable	Borderline Low	Low
HDL–C	>45	40–44	<40

*Values provided are from the Lipid Research Clinics Prevalence Study. The cut points for TC, LDL–C, and non-HDL–C represent the 95th percentile for subjects ages 20–24 years and are not identical with the cut points used in the most recent (2001) National Cholesterol Education Program's Adult Treatment Panel III, which are derived from combined data on adults of all ages. The age-specific cut points given here are provided for pediatric care providers to use in managing this young adult age group. For TC, LDL–C, and non-HDL–C, borderline high values are between the 75th and 94th percentiles, whereas acceptable values are <75th percentile. The high TG cut point represents approximately the 90th percentile, with borderline high between the 75th and 89th percentiles; acceptable is <75th percentile. The low HDL–C cut point represents roughly the 25th percentile, with borderline low between the 26th and 50th percentiles; acceptable is >50th percentile.

Conclusions and Grading of the Evidence Review for Lipid Assessment

- Combined evidence from autopsy studies, vascular studies, and cohort studies strongly indicates that abnormal lipid levels in childhood are associated with increased evidence of atherosclerosis (Grade B).
- The evidence review supports the concept that early identification and control of dyslipidemia throughout youth and into adulthood will substantially reduce clinical cardiovascular disease (CVD) risk beginning in young adult life. Preliminary evidence in children with heterozygous familial hypercholesterolemia (FH) with markedly elevated LDL–C indicates that earlier treatment is associated with reduced subclinical evidence of atherosclerosis (Grade B).
- Multiple prospective screening cohort studies have demonstrated the normal lipid and lipoprotein distributions in childhood, adolescence, and young adult life (see Table 9–1 in the original guideline document and the table "Recommended Cut Points for Lipid and Lipoprotein Levels [mg/dL] in Young Adults," above) (Grade B).
- Cohort studies have also demonstrated significant tracking of elevated lipid levels from childhood to adulthood, with lipid and lipoprotein results in childhood predictive of future adult lipoprotein profiles; the strongest statistical correlation occurs between results in late childhood and the third and fourth decades of life (Grade B).
- TC and LDL–C levels fall as much as 10–20 percent or more during puberty (Grade B). Based on this normal pattern of change in lipid and lipoprotein levels with growth and maturation, age 10 years (age range 9–11 years) is a stable time for lipid assessment in children (Grade D). For most children, this age range will precede onset of puberty.
- Significant evidence exists that using family history of premature CVD or of cholesterol disorders as the primary factor in determining lipid screening for children misses approximately 30–60 percent of children with dyslipidemias, and accurate and reliable measures of family history are not available (Grade B). In the absence of a clinical or historic marker, identification of children with lipid disorders that predispose them to accelerated atherosclerosis requires universal lipid assessment (Grade D).
- Non-HDL–C has been identified as a significant predictor of the presence of atherosclerosis, as powerful as any other lipoprotein cholesterol measure in children and adolescents. For both children and adults, non-HDL–C appears to be more predictive of persistent dyslipidemia, and therefore atherosclerosis and future events, than TC, LDL–C, or HDL–C alone. A major advantage of non-HDL–C is that it can be accurately calculated in a nonfasting state and is therefore very practical to obtain in clinical practice. The evidence supports use of non-HDL–C as a screening tool for identification of a dyslipidemic state in childhood (Grade B).
- In terms of other lipid measurements: (1) at this time, most but not all studies indicate that measurement of apolipoprotein B (apoB) and apolipoprotein A-1 (apoA–1) for universal screening provides no additional advantage over measuring non-HDL–C, LDL–C, and HDL–C; (2) measurement of lipoprotein(a) (Lp[a]) is useful in the assessment of children with both hemorrhagic and ischemic stroke; (3) in offspring of a parent with premature CVD and no other identifiable risk factors, elevations of apoB, apoA–1, and Lp(a) have been noted; and (4) measurement of lipoprotein subclasses and their sizes by advanced lipoprotein testing has not been shown to have sufficient clinical utility in

children at this time (Grade B).

- Obesity is commonly associated with a combined dyslipidemia pattern, with mild elevations in TC and LDL–C, moderate to severe elevation in TG, and low HDL–C. This is the most common dyslipidemic pattern seen in childhood, and lipid assessment of overweight and obese children identifies an important proportion with significant lipid abnormalities (Grade B).
- Dyslipidemias can be acquired genetically but also secondary to specific conditions, such as diabetes, nephrotic syndrome, chronic renal disease, postorthotopic heart transplant, history of Kawasaki disease with persistent coronary involvement, chronic inflammatory disease, hypothyroidism, and other causes, as outlined in Table 9–3 in the original guideline document. There is impressive evidence for accelerated atherosclerosis both clinically and as assessed with noninvasive methods in some of these conditions, which accordingly have been designated as special risk diagnoses for accelerated atherosclerosis (see Table 9–7 in the original guideline document); management of these is described in the NGC summary Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis. Lipid evaluation of these patients contributes to risk assessment and identifies an important proportion with dyslipidemia (Grade B).
- The complete phenotypic expression of some inherited disorders, such as familial combined hyperlipidemia (FCHL), may be delayed until adulthood. Evaluation in children and adolescents from high-risk families with FCHL that begins in childhood and continues through adulthood (per NCEP adult treatment guidelines) will lead to early detection of those with abnormalities (Grade B).

Age-specific recommendations for lipid assessment are outlined in the table below. Specific management for children with identified dyslipidemia is outlined in the algorithms in Figures 9–1 and 9–2 in the original guideline document. Definitions of the risk factors and special risk conditions for use with the recommendations and in the algorithms appear in Tables 9–6 and 9–7 in the original guideline document. The advantages of identifying dyslipidemia and initiating treatment in childhood are the potential for increased reversibility or slowing of the disease process, the knowledge that lifestyle change and attention to risk are more readily accomplished than with individuals in their twenties and thirties, and the fact that regular contact with the health care system is routine in this age group. Late adolescence is often the last time for many years that young adults will routinely undergo health assessment, at the precollege or preemployment physical. It therefore represents an opportunity to diagnose lipid disorders and to advise the young adult about his or her cardiovascular (CV) risk profile and a healthy lifestyle pattern. When medication is recommended, the decision occurs in the context of the complete CV risk profile of the patient and the sociocultural milieu of the family.

The first step proposed for management of children with identified lipid abnormalities is a focused intervention to improve diet and physical activity. Conclusions of the evidence review and recommendations for dietary management of dyslipidemias are provided below.

Evidence-Based Recommendations for Lipid Assessment

Grades reflect the findings of the evidence review.

Recommendation levels reflect the consensus opinion of the Expert Panel.

NOTE: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL–C), high-density lipoprotein cholesterol (HDL–C), and non-HDL–C by 38.6; for triglycerides (TG), divide by 88.6.

Birth–2 years	No lipid screening	Grade C *Recommend*
2–8 years	No routine lipid screening	Grade B *Recommend*
	Measure fasting lipid profile (FLP) × 2*; average results** if: • Parent, grandparent, aunt/uncle, or sibling with myocardial infarction (MI), angina, stroke, coronary artery bypass graft (CABG)/stent/angioplasty at <55 years in males, <65 years in females *Interval between FLP measurements: after 2 weeks but within 3 months. **Use Table 9–1 in the original guideline document for interpretation of results; use lipid algorithms in Figures 9–1 and 9–2 in the original guideline document for management of results.	Grade B *Strongly recommend*
	• Parent with TC ≥240 mg/dL or known dyslipidemia	Grade B *Strongly recommend*

	• Child has diabetes, hypertension, body mass index (BMI) ≥95th percentile or smokes cigarettes	Grade B *Strongly recommend*
	• Child has a moderate- or high-risk medical condition (see Table 9-7 In the original guideline document)	Grade B *Strongly recommend*
9–11 years	Universal Screening • Non-FLP: Calculate non-HDL-C: Non HDL C = TC - HDL C* Non-HDL ≥145 mg/dL, HDL< 40 mg/dL →FLP × 2, lipid algorithms (see original guideline document)** OR • FLP: LDL-C ≥130 mg/dL, non-HDL-C ≥145 mg/dL HDL-C <40 mg/dL, TG ≥100 mg/dL if < 10 years; ≥130 mg/dL if ≥10 years → Repeat FLP after 2 weeks but within 3 months → lipid algorithms in the original guideline document** *Disregard TG and LDL-C in nonfasting sample. **Use Table 9–1 in the original guideline document for interpretation of results; use lipid algorithms in Figures 9–1 and 9–2 in the original guideline document for management of results.	Grade B *Strongly recommend*
12–16 years	No routine screening* *Lipid screening is not recommended for those aged 12–16 years because of significantly decreased sensitivity and specificity for predicting adult LDL–C levels and significantly increased false-negative results in this age group. Selective screening is recommended for those with the clinical indications outlined.	Grade B *Recommend*
	Measure FLP × 2**, average results, if new knowledge of: • Parent, grandparent, aunt/uncle or sibling with MI, angina, stroke, CABG/stent/angioplasty, sudden death at <55 years in males, <65 years in females **Interval between FLP measurements: after 2 weeks but within 3 months.	Grade B *Strongly recommend*
	• Parent with TC ≥240 mg/dL or known dyslipidemia	Grade B *Strongly recommend*
	• Patient has diabetes, hypertension, BMI ≥85th percentile or smokes cigarettes	Grade B *Strongly recommend*
	• Patient has a moderate- or high-risk medical condition (see Table 9–7 in the original guideline document)	Grade B *Strongly recommend*
17–21 years	Universal screening once in this time period: Non-FLP: Calculate non-HDL–C: Non-HDL–C = TC – HDL–C* 17–19 years: Non-HDL–C ≥145 mg/dL, HDL–C<40 mg/dL	Grade B *Recommend*

	→FLP × 2, lipid algorithm (Figure 9–1 in the original guideline) OR FLP: LDL–C ≥130 mg/dL, non-HDL–C ≥145 mg/dL HDL–C <40 mg/dL, TG ≥130 mg/dL → Repeat FLP after 2 weeks but within 3 months→ lipid algorithms in Figures 9–1 and 9–2 in the original guideline 20–21 years: Non-HDL–C ≥190 mg/dL, HDL–C <40 mg/dL** → FLP ×2† average results → *Adult Treatment Panel III (ATP III)* management algorithm OR FLP: LDL–C ≥160 mg/dL, non-HDL–C ≥190 mg/dL HDL–C <40 mg/dL, TG ≥150 mg/dL → Repeat FLP after 2 weeks but within 3 months, average results → *ATP III* management algorithm *Use Table 9–1 in the original guideline document for interpretation of results of 7- to 19-year-olds and lipid algorithms in Figures 9–1 and 9–2 in the original guideline for management. Use the table above, Recommended Cut Points for Lipid and Lipoprotein Levels (mg/dL) in Young Adults, for interpretation of results of 20- to 21-year-olds and *ATP III* algorithms for management. **Disregard TG and LDL-C in nonfasting sample. †Interval between FLP measurements: after 2 weeks but within 3 months.	

Conclusions and Grading of the Evidence Review for Dietary Management of Dyslipidemia

- A diet with total fat at 25–30 percent of calories, saturated fat less than 10 percent of calories, and cholesterol intake less than 300 mg/d, as recommended by the original NCEP Pediatric Panel, has been shown to safely and effectively reduce the levels of TC and LDL–C in healthy children (Grade A). There is some evidence this is also the case when the diet begins in infancy and is sustained throughout childhood into adolescence (Grade B). The Cardiovascular Health Integrated Lifestyle Diet (CHILD 1), described in the NGC summary Nutrition and Diet, has this composition.
- In children with identified hypercholesterolemia and elevated LDL–C levels, a more stringent diet, with saturated fat <7 percent of calories and dietary cholesterol limited to 200 mg/d, has been shown to be safe and modestly effective in lowering LDL–C levels (CHILD 2-LDL, see table below) (Grade A).
- Use of dietary adjuncts, such as plant sterol or stanol esters, up to 2 g/d can safely enhance the LDL–C-lowering effects short term in children with familial hypercholesterolemia (FH) (Grade A). However, long-term studies on the safety and effectiveness of plant sterol and stanol esters have not been completed. Their clinical use is therefore usually reserved for children with primary elevations of LDL–C who do not achieve LDL–C goals with dietary treatment alone. Such an approach may lower LDL–C sufficiently to avoid the necessity of drug treatment. Food products containing plant stanol esters, such as some margarines, are marketed directly to the general public. In two short-term trials, they have been shown to be safe with minimal LDL-lowering effects in healthy children (Grade B).
- Evidence for use of other dietary supplements is insufficient for any recommendation (no grade).
- In children with elevated TG, weight loss and reduction of simple carbohydrate intake are associated with decreased TG levels (CHILD 2-TG, see table below) (Grade B). When elevated TG are associated with obesity, decreased calorie intake and increased activity levels are of paramount importance.
- A behavioral approach that engages the child and family delivered by a registered dietitian has been shown to be the most consistently effective approach for achieving dietary change (Grade B).

The approach to management of dyslipidemias is staged, as in the original NCEP Pediatric Panel recommendations. For all children with identified dyslipidemia in whom the response to a low-fat/low saturated fat/low cholesterol diet has not been evaluated, the CHILD 1 diet described in the NGC summary of Nutrition and Diet is recommended as the first step, with implementation guided by a registered dietitian. For obese children with identified dyslipidemia, age- and BMI-specific additional recommendations addressing calorie restriction and increased activity appear in the NGC summary Overweight and Obesity. If, after a 3-month trial of CHILD 1/lifestyle management, fasting lipid profile findings exceed the therapeutic goals in Table 9-1 of the original guideline and in the table above (Recommended Cut Points for Lipid and Lipoprotein Levels (mg/dL) in Young Adults), lipid parameter-specific diet changes outlined in the table below are recommended. Dyslipidemia management is also outlined in the algorithms in Figures 9–1 and 9–2 in the original guideline document.

Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, non–HDL-C and TG

Grades reflect the findings of the evidence review.

Recommendation levels reflect the consensus opinion of the Expert Panel.

Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

NOTE: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Elevated LDL–C: CHILD 2 - LDL		
2–21 years	Refer to a registered dietitian for family medical nutrition therapy:	Grade B *Strongly recommend*
	• 25%–30% of calories from fat, ≤7% from saturated fat, ~10% from monounsaturated fat; <200 mg/d of cholesterol; avoid trans fats as much as possible	Grade A *Recommend*
	Supportive actions: • Plant sterol esters and/or plant stanol esters* up to 2 g/d as replacement for usual fat sources can be used after age 2 years in children with familial hypercholesterolemia. • Plant stanol esters as part of a regular diet are marketed directly to the public. Short-term studies show no harmful effects in healthy children. • The water-soluble fiber psyllium can be added to a low-fat, low saturated fat diet as cereal enriched with psyllium at a dose of 6 g/d for children 2–12 years, and 12 g/d for those ≥12 years. • As in all children, 1 h/d of moderate to vigorous physical activity and <2 h/d of sedentary screen time are recommended. *Can be found added to some foods, such as some margarines	
Elevated TG or Non-HDL–C: CHILD 2 – TG		
2–21 years	Refer to a registered dietitian for family medical nutrition therapy:*	Grade B *Recommend*
	• 25%–30% of calories from fat, ≤7% from saturated fat, ~10% from monounsaturated fat; <200 mg/d of cholesterol; avoid trans fats as much as possible	Grade A *Recommend*

	• Decrease sugar intake:
	  • Replace simple with complex carbohydrates
	  • No sugar sweetened beverages
		Grade B *Recommend*

	• Increase dietary fish to increase omega-3 fatty acids**	Grade D *Recommend*
	*If child is obese, nutrition therapy should include calorie restriction, and increased activity (beyond that recommended for all children) should be prescribed. See the NGC summary Overweight and Obesity for additional age-specific recommendations. **The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are low in mercury. For more information, call the FDA's food information line toll free at 1–888–SAFEFOOD or visit http://www.fda.gov/Food/default.htm.	

Conclusions and Grading of the Evidence Review for Use of Medication to Treat Dyslipidemia

When medication is recommended, this should always be in the context of the complete CV risk profile of the patient and in consultation with the patient and the family.

NOTE: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

- Decisions regarding the need for medication therapy should be based on the average of results from at least two fasting lipid profiles obtained at least 2 weeks but no more than 3 months apart (Grade C) (see Figure 9–1 in the original guideline document).
- The cut points used to define the level at which drug therapy should be considered from the 1992 *NCEP Pediatric Guidelines* have been used as the basis for multiple drug safety and efficacy trials in dyslipidemic children (Grade B):
  - LDL–C ≥190 mg/dL after a 6-month trial of lifestyle management (CHILD 1→CHILD 2-LDL) for children ages ≥10 years.
  - LDL–C 160–189 mg/dL after a 6-month trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL) in a child ≥age 10 years with a positive family history of premature CVD/events in first-degree relatives (Table 9–6) or at least one high-level risk factor or risk condition or at least 2 moderate-level risk factors or risk conditions (see Tables 9–6, 9–7 in the original guideline and table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below) (see also Figure 9–1 in the original guideline).
  - LDL–C 130–190 mg/dL in a child ≥age 10 years with a negative family history of premature CVD in first-degree relatives and no high-level or moderate-level risk factor or risk condition, management should continue to focus on lifestyle changes (CHILD 1→CHILD 2-LDL) based on lipid profile findings (see Figure 9–1 in the original guideline) plus weight management if BMI is at least the 85th percentile.
  - The goal of LDL-lowering therapy in childhood and adolescence is LDL–C below the 95th percentile (≤130 mg/dL).
- Children with homozygous FH and extremely elevated LDL–C levels (>500 mg/dL) have undergone effective LDL-lowering therapy with biweekly LDL apheresis under the care of lipid specialists in academic medical centers (Grade C).
- Multiple cohort studies have shown benefits of LDL-lowering therapy in children at high risk for accelerated atherosclerosis (see Table 9–7 in the original guideline). Children and adolescents with chronic kidney disease, type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM), Kawasaki disease with coronary aneurysms, or postcardiac transplantation should be considered for initiation of medication therapy (Grade C) (see the NGC summary of Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis).
- The bile acid sequestrants are medications that bind bile salts within the intestinal lumen and prevent their enterohepatic reuptake in the terminal ileum, resulting in a depletion of bile salts in the liver and a signal for increased production. Since bile salts are synthesized from intracellular cholesterol in the liver, the intracellular pool of cholesterol becomes depleted, signaling increased production of LDL receptors and increased clearance of circulating LDL–C to replenish the intracellular cholesterol pool for increased production of bile salts. Studies of bile acid sequestrants in children and adolescents ages 6–18 years with LDL–C levels from 131 to 190 mg/dL show TC reduction of 7-17 percent and reduction of LDL–C of 10–20 percent, sometimes with a modest elevation in TG levels. The bile acid sequestrants commonly have gastrointestinal side effects, and these significantly affect compliance. However, they are safe and moderately effective (Grade A).
- Statin medications inhibit hydroxymethylglutaryl coenzyme A reductase, which is a rate-limiting enzyme in the endogenous cholesterol synthesis pathway. This results in a decrease in the intracellular pool of cholesterol, which signals upregulation of LDL receptors and increased clearance of circulating LDL–C. As a group, statins have been shown to reduce LDL–C in children and adolescents with marked LDL–C elevation or FH (defined as elevated LDL–C in the child in conjunction with a family history of elevated LDL–C and/or atherosclerosis or CAD) when used from 8 weeks to 2 years for children ages 8–18 years. The lower LDL–C level for eligibility into the statin trials was ≥190 mg/dl or ≥160 mg/dl with 2 or more additional risk factors, after a trial period on diet. Trial subjects were monitored carefully throughout treatment; adverse impacts on growth, development, or sexual maturation were not seen, and adverse event profiles and efficacy were similar to those in studies of adults (Grade A).
- Adverse effects from statins are rare at standard doses but include myopathy and hepatic enzyme elevation. In the meta-analysis of statin use in children, evidence of hepatic enzyme elevation and muscle toxicity did not differ between the statin and placebo groups. Routine monitoring of hepatic enzymes and clinical assessment for muscle toxicity are strongly recommended for children and adolescents on statin therapy (see table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below). The risk of adverse events increases with use of higher doses and interacting drugs, the latter occurring primarily with drugs that are metabolized by the cytochrome P–450 system, which is the primary mode of metabolism for the majority of statins. Drugs that potentially interact with statins include fibrates, azole antifungals, macrolide antibiotics, antiarrhythmics, and protease inhibitors (Grade A).
- Bile acid-binding sequestrants may be used in combination with a statin for patients who fail to meet LDL–C target levels with either medication alone. One pediatric study assessed this combination and showed no increase in adverse effects. The efficacy of the two agents together appears to be additive (Grade B).

- There is limited published experience in children with use of niacin and fibrates, which have been useful in treating adult patients with combined dyslipidemias. Efficacy and safety data are limited, and no data are available regarding newer formulations. In adults, cholesterol absorption inhibitors have been advocated as an adjunct to statin therapy for patients who do not reach LDL–C therapeutic targets. Since their action is independent of and complementary to that of statins, the LDL–C-lowering effect is additive. No pediatric studies of monotherapy with cholesterol absorption inhibitors had been published during the time period for this evidence review. Use of niacin, fibrates, and cholesterol absorption inhibitors should be instituted only in consultation with a lipid specialist (Grade C).
- Medication therapy is rarely needed for children with elevated TG who respond well to weight loss and lifestyle changes (Grade B). When TG levels exceed 500 mg/dL, patients are at risk for pancreatitis and require care in consultation with a lipid specialist (Grade B). In adults, use of omega-3 fish oil has been shown to lower TG by 30–40 percent and to raise HDL by 6–17 percent. Experience with fish oil in children is limited to small case series with no safety concerns identified; there have been no RCTs of fish oil in children (Grade D).

Age-Based Recommendations for Medication Therapy of Children with Dyslipidemia

Children Younger Than Age 10 Years

- Children younger than age 10 years should not be treated with a medication unless they have a severe primary hyperlipidemia or a high-risk condition that is associated with serious medical morbidity (homozygous hypercholesterolemia/LDL–C ≥400 mg/dL; primary hypertriglyceridemia with TG ≥500 mg/dL; evident CVD in the first two decades of life; post cardiac transplantation) (Grade C).

Children Ages 10–21 Years (see algorithms, Figures 9–1 and 9–2 in the original guideline document)

- Decisions regarding the need for medication therapy should be based on the average of results from ≥2 FLPs obtained at least 2 weeks but no more than 3 months apart (Grade C) (see Figure 9–1 in the original guideline document).
- Children with average LDL–C ≥250 mg/dL or average TG ≥500 mg/dL should be referred directly to a lipid specialist (Grade B).
- Children with lipid abnormalities should have a detailed family history taken and be assessed for causes of hyperlipidemia, additional risk factors, and risk conditions (Grade C) (see Tables 9–3, 9–6, and 9–7 in the original guideline document).
- Children with lipid abnormalities (other than LDL–C ≥250 mg/dL or TG ≥500 mg/dL) should be initially managed for 3–6 months with diet changes (CHILD 1→CHILD 2-LDL or CHILD 2-TG; see table "Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, non-HDL-C and TG" above) based on specific lipid profile findings (see Figures 9–1 and 9–2 in the original guideline document); if BMI is ≥85th percentile, add increased physical activity, reduce screen time, and restrict calories. Assessment for associated secondary causes (see Table 9–3 in the original guideline document), additional risk factors, or high-risk conditions (Tables 9–6 and 9–7 in the original guideline) is recommended. Children at high risk who are unlikely to achieve lipid targets with this strategy alone (severe primary dyslipidemia, cardiac transplantation) should concomitantly be considered for initiation of medication therapy (Grade C) (see the NGC summary Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis).

LDL–C: Treatment for Children with Severe Elevation of LDL–C Is Based on Assessment of Lipid Levels and Associated Risk Factors or Risk Conditions (see Tables 9–6 and 9–7; Figures 9–1 and 9–2 in the original guideline document)

- Children with average LDL–C ≥250 mg/dL should be referred directly to a lipid specialist (Grade B).
- If LDL–C remains ≥190 mg/dL after a 6-month trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL) for children ages 10 years and older, statin therapy should be considered (Grade A) (see Figure 9–1 in original guideline document and table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).
- If LDL–C remains 130–190 mg/dL in a child age 10 years or older with a negative family history of premature CVD in first-degree relatives and no high-level or moderate-level risk factor or risk condition (see Tables 9–6 and 9–7 in the original guideline document), management should continue to focus on diet changes (CHILD 2-LDL) based on lipid profile findings (see Figure 9–1 in the original guideline document) plus weight management if BMI is ≥85th percentile. Pharmacologic therapy is not generally indicated, but treatment with bile acid sequestrants might be considered, the latter in consultation with a lipid specialist (Grade B).
- If LDL–C remains 160–189 mg/dL after a trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL) in a child age 10 years or older with a positive family history of premature CVD/events in first-degree relatives (see Table 9–6 in the original guideline document) or at least one high-level risk factor or risk condition or at least two moderate-level risk factors or risk conditions (see Tables 9–6 and 9–7 in the original guideline document), then statin therapy should be considered (Grade B) (see Figure 9–1 and Table 9–12 in the original guideline document).
- If LDL–C remains ≥130 to 159 mg/dL after a trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL) in a child age 10 years or older with at least two high-level risk factors or risk conditions or at least one high-level risk factor or risk condition together with at least two moderate-level risk factors or risk conditions (see Tables 9–6 and 9–7 in the original guideline document), then statin therapy should be considered (Grade C) (see Figure 9–1 in the original guideline document and table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).

- For children ages 8 and 9 years with LDL–C persistently ≥190 mg/dL after a trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL), together with multiple first-degree family members with premature CVD/events, or the presence of at least one high-level risk factor or risk condition or the presence of at least two moderate-level risk factors or risk conditions (see Figure 9–1 and Tables 9–6 and 9–7 in the original guideline document), statin therapy might be considered (Grade B) (see table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).
- Statin use should begin with the lowest available dose given once daily. If LDL–C target levels are not achieved with at least 3 months of compliant use, then the dose may be increased by one increment (usually 10 mg). If LDL–C target levels are still not achieved with at least 3 months of compliant use, then the dose may be further increased by one increment. The risk and effectiveness of dose escalation has been explored in several of the statin clinical trials in children with no additional safety issues identified (Grade B). Alternatively, a second agent such as a bile acid sequestrant or cholesterol absorption inhibitor may be added under the direction of a lipid specialist (Grade B) (see table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).
- Children taking a statin should have routine clinical monitoring for symptoms of muscle toxicity and assessment of hepatic transaminases and creatine kinase (Grade A) (see table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).
- Pediatric care providers should be on the alert for, and children and their families should be counseled about, potential medication interactions (Grade D) (see table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).
- Females taking a statin should be counseled about risks associated with pregnancy and appropriate contraception strategies if indicated. Use of oral contraceptives in combination with statins is not contraindicated (Grade D) (see table "Recommendations for Use of HMG CoA Reductase Inhibitors [Statins] in Children and Adolescents" below).

TG, non-HDL–C: Children with Elevated TG or Elevated Non-HDL–C after Control of LDL–C Are Managed Based on Lipid Levels (see Figure 9–2 in the original guideline document):

- Children with average fasting levels of TG ≥500 mg/dL or any single measurement ≥1,000 mg/dL related to a primary hypertriglyceridemia should be treated in conjunction with a lipid specialist; the CHILD 2-TG diet (see table "Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, Non-HDL–C, and TG" above) should be started and use of fish oil, fibrate, or niacin to prevent pancreatitis should be considered (Grade D) (see Figure 9–2 and Tables 9–10 and 9–11 in the original guideline document.)
- Children with fasting levels of TG 200–499 mg/dL after a trial of lifestyle/diet management with CHILD 1→CHILD 2-TG (see table "Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, Non-HDL–C, and TG" above) should have non-HDL recalculated and be managed to a goal of less than 145 mg/dL (Grade D).
- Children with fasting levels of TG 200–499 mg/dL, non-HDL ≥145 mg/dL, after a trial of lifestyle/diet management with CHILD 1→CHILD 2-TG (see table "Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, Non-HDL–C, and TG" above), including increased fish intake, may be considered for fish oil supplementation (Grade D) (see Table 9–10 in the original guideline document).
- Children ages 10 years or older with non-HDL–C levels ≥145 mg/dL after the LDL–C goal is achieved may be considered for further intensification of statin therapy or additional therapy with a fibrate or niacin, in conjunction with referral to a lipid specialist (Grade D) (see Figure 9–1 and Tables 9–10 and 9–11 in the original guideline document).
- Children with severe or complex mixed dyslipidemias, particularly where multiple medications are being considered, should be referred for consultation with a lipid specialist (Grade D) (see Figures 9–1 and 9–2 in the original guideline document).

The age-specific recommendations for pharmacologic management of dyslipidemia are summarized in the table the table below.

Evidence-Based Recommendations for Pharmacologic Treatment of Dyslipidemia

Grades reflect the findings of the evidence review.

Recommendation levels reflect the consensus opinion of the Expert Panel.

When medication is recommended, this should always be in the context of the complete cardiovascular risk profile of the patient and in consultation with the patient and the family.

NOTE: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Birth–	Pharmacologic treatment is limited to children with severe primary hyperlipidemia (homozygous familial	Grade C

10 years	hypercholesterolemia, primary hypertriglyceridemia with TG ≥500 mg/dL) or a high-risk condition (see Tables 9–6 and 9–7 in the original guideline document) or evident cardiovascular disease; all under the care of a lipid specialist.	*Recommend*
≥10–21 years	Detailed family history (FHx) and risk factor (RF) assessment required before initiation of drug therapy.* High- to moderate-level RFs and risk conditions (RCs) in Tables 9–6 and 9–7 in the original guideline document.	Grade C *Strongly recommend*
	LDL–C:	
	If average LDL–C ≥250 mg/dL*, consult lipid specialist.	Grade B *Strongly recommend*
	If average LDL–C ≥130–250 mg/dL, or non-HDL ≥145 mg/dL: • Refer to dietitian for medical nutrition therapy with Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) → CHILD 2-LDL (see table "Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, Non-HDL–C, and TG" above) × 6 months → repeat fasting lipid panel (FLP)	Grade A *Strongly recommend*
	Repeat FLP:	
	• → LDL–C <130 mg/dL, continue CHILD 2- LDL, reevaluate in 12 months	Grade A *Strongly recommend*
	• → LDL–C ≥190** mg/dL, consider initiation of statin therapy per Table 9–11 in the original guideline document and table "Recommendations for Use of HMG CoA Reductase Inhibitors (Statins) in Children and Adolescents" below.	Grade A *Strongly recommend*
	• →LDL–C ≥130–189 mg/dL, FHx (-), no other RF or RC, continue CHILD 2-LDL, reevaluate q. 6 months	Grade B *Recommend*
	• → LDL–C = 160–189 mg/dL + FHx positive OR ≥1 high-level RF/RC OR ≥2 moderate-level RFs/RCs, consider statin therapy per Table 9–11 in the original guideline document and table "Recommendations for Use of HMG CoA Reductase Inhibitors (Statins) in Children and Adolescents" below.	Grade B *Recommend*
	• → LDL–C ≥130–159 mg/dL + ≥2 high-level RFs/RCs OR 1 high-level + 2 moderate-level RFs/RCs, consider statin therapy per Table 9–11 in the original guideline document and table "Recommendations for Use of HMG CoA Reductase Inhibitors (Statins) in Children and Adolescents" below.	Grade B *Recommend*
	Children on statin therapy should be counseled and carefully monitored per table "Recommendations for Use of HMG CoA Reductase Inhibitors (Statins) in Children and Adolescents" below.	Grade A *Strongly recommend*
	Detailed FHx and RF/RC assessment required before initiation of drug therapy.* High- and moderate-level RFs/RCs in Tables 9–6 and 9–7† in the original guideline document.	Grade C *Strongly recommend*
	TG:	
	If average TG ≥500 mg/dL, consult lipid specialist	Grade B *Recommend*
	If average TG ≥100 mg/dL in a child <10 years, ≥130 mg/dL in a child age 10–19 years, <500 mg/dL:	
	• Refer to dietitian for medical nutrition therapy with CHILD 1 → CHILD 2-TG (see table "Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, non-HDL-C and TG" above) × 6 months	Grade B *Strongly*

		recommend
	Repeat fasting lipid profile:	
	• → TG <100 (130) mg/dL, continue CHILD 2-TG, monitor q. 6–12 months	Grade B *Strongly recommend*
	• → TG >100 (130) mg/dL, reconsult dietitian for intensified CHILD 2-TG diet counseling	Grade C *Recommend*
	• → TG ≥200–499 mg/dL, non-HDL ≥145 mg/dL, consider fish oil +/- consult lipid specialist	Grade D *Recommend*
	Non-HDL-C:	
	Children ≥10 years with non-HDL–C ≥145 mg/dL after LDL–C goal achieved may be considered for additional treatment with statins, fibrates, or niacin in conjunction with a lipid specialist.	Grade D *Optional*

*Consideration of drug therapy based on the average of ≥2 FLPs, obtained at least 2 weeks but no more than 3 months apart.

**If average LDL–C ≥190 mg/dL after CHILD 2-LDL and child is age 8–9 years with + FHx OR ≥1 high-level RF/RC OR ≥ 2 moderate-level RFs/RCs, statin therapy may be considered.

†If child is obese, nutrition therapy should include calorie restriction and increased activity beyond that recommended for all children. See the NGC summary of Overweight and Obesity for additional age-specific recommendations in the integrated guidelines.

Recommendations for Use of Hydroxy-3-Methyl-Glutaryl Coenzyme A (HMG CoA) Reductase Inhibitors (Statins) in Children and Adolescents

Patient Selection
1. Use algorithm (see Figure 9–1 in the original guideline document) and risk factor categories (see Tables 9–6 and 9–7 in the original guideline document) to select statin therapy for patients. 2. Include preferences of patient and family in decision making. 3. In general, do not start treatment with statins before age 10 years (patients with high-risk family history, high-risk conditions, or multiple risk factors [see Tables 9–6 and 9–7 in the original guideline document] might be considered for medication initiation at age 10 years or younger.) 4. Precaution/contraindication with potentially interactive medications (cyclosporine, niacin, fibric acid derivatives, erythromycin, azole antifungals, nefazodone, many human immunodeficiency virus [HIV] protease inhibitors). Check for potential interaction with all current medications at baseline. 5. Conduct baseline hepatic panel and creatine kinase (CK) before initiating treatment.
Initiation and Titration
1. Choice of particular statin is a matter of preference. Clinicians are encouraged to develop familiarity and experience with one of the statins, including dosage regimen and potential drug-drug interactions. 2. Start with the lowest dose once daily, usually at bedtime. Atorvastatin and rosuvastatin can be taken in the morning or evening because of their long half-lives. 3. Measure baseline CK, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). 4. Instruct the patient to report all potential adverse effects, especially muscle cramps, weakness, asthenia, and more diffuse symptoms suggestive of myopathy. 5. Advise female patients about concerns with pregnancy and the need for appropriate contraception. 6. Advise about potential future medication interactions, especially cyclosporine, niacin, fibric acid derivatives, erythromycin, azole antifungals, nefazodone, and HIV protease inhibitors. Check for potential interaction whenever any new medication is initiated. 7. Whenever potential myopathy symptoms present, stop medication and assess CK; determine relation to recent physical activity. The

threshold for worrisome level of CK is 10 times above the upper limit of reported normal, considering the impact of physical activity. Monitor the patient for resolution of myopathy symptoms and any associated increase in CK. Consideration can be given to restarting the medication once symptoms and laboratory abnormalities have resolved.

8. After 4 weeks, measure fasting lipid profile (FLP), ALT, and AST and compare with laboratory-specific reported normal values.
    - The threshold for worrisome levels of ALT or AST is ≥3 times the upper limit of reported normal.
    - Target levels for low-density lipoprotein cholesterol (LDL–C): minimal <130 mg/dL; ideal <110 mg/dL.
9. If target LDL–C levels are achieved and there are no potential myopathy symptoms or laboratory abnormalities, continue therapy and recheck FLP, ALT, and AST in 8 weeks and then 3 months.
10. If laboratory abnormalities are noted or symptoms are reported, temporarily withhold the medication and repeat the blood work in 2 weeks. When abnormalities resolve, the medication may be restarted with close monitoring.
11. If target LDL-C levels are not achieved, increase the dose by one increment (usually 10 mg) and repeat the blood work in 4 weeks. If target LDL-C levels are still not achieved, dose may be further increased by one increment or another agent (bile acid sequestrant or cholesterol absorption inhibitor) may be added under the direction of a lipid specialist.

Maintenance Monitoring

1. Monitor growth (height, weight, and body mass index [BMI] relative to normal growth charts), sexual maturation, and development.
2. Whenever potential myopathy symptoms present, stop medication and assess CK.
3. Monitor fasting lipoprotein profile, ALT, and AST every 3-4 months in the first year, every 6 months in the second year and beyond, and whenever clinically indicated.
4. Monitor and encourage compliance with lipid-lowering dietary and medication therapy. Serially assess and counsel for other risk factors, such as weight gain, smoking, and inactivity.
5. Counsel adolescent females about statin contraindications in pregnancy and the need for abstinence or use of appropriate contraceptive measures. Use of oral contraceptives is not contraindicated if medically appropriate. Seek referral to an adolescent medicine or gynecologic specialist as appropriate.

Definitions:

Evidence Quality for Grades of Evidence

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the Guidelines' target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies

Guidelines' Definitions for Evidence-Based Statements

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent (Grade A or B). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade C or D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel believes that the benefits exceed the harms but the quality of the evidence is not as strong (Grade B or C). In some clearly defined	Clinicians should generally follow a recommendation but remain alert to new

Statement Type	Definition	Implication
	circumstances, strong recommendations may be made on the basis of lesser evidence (Grade D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and family preferences should have a substantial influencing role.
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and should be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preferences should have a substantial influencing role.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Dyslipidemia Algorithm: TARGET Low-Density Lipoprotein Cholesterol
- Dyslipidemia Algorithm: TARGET Triglycerides

Scope

Disease/Condition(s)

- Atherosclerotic cardiovascular disease
- Cardiovascular health
- Dyslipidemia

Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Family Practice

Internal Medicine

Nursing

Nutrition

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide comprehensive evidence-based guidelines addressing the known risk factors for cardiovascular disease (CVD)
- To assist all pediatric care providers in both the promotion of cardiovascular (CV) health and the identification and management of specific risk factors from infancy into young adulthood
- To provide recommendations to pediatric care providers on lipid management in their patients

Target Population

- Children and adolescents in the general population and their parents/guardians
- Children and adolescents with confirmed dyslipidemias and their parents/guardians

Interventions and Practices Considered

1. Lipid screening (fasting lipid panel, non-fasting lipid panel) based on age and personal and family risk factors
2. Referral to registered dietitian for medical nutrition therapy
3. Restricting fat (including saturated and monosaturated fats) and cholesterol intake
4. Decreasing sugar intake
5. Increasing dietary fish intake to increase omega-3 fatty acids
6. Lifestyle and diet management of dyslipidemia (Cardiovascular Health Integrated Lifestyle Diet [CHILD])
7. Detailed family history and risk factor assessment before initiation of drug therapy for dyslipidemia
8. Obtaining at least two lipid panels separated by at least 2 weeks and no more than 3 months before initiating drug therapy
9. Drug therapy with bile sequestrants, statins
10. Use of niacin, fibrates, and cholesterol absorption inhibitors in conjunction with a lipid specialist
11. Monitoring lipid levels during therapy
12. Monitoring liver function and adverse effects of statin therapy

Major Outcomes Considered

Blood lipid level:

- Total cholesterol
- Triglycerides
- High-density lipoprotein cholesterol (HDL–C)
- Low-density lipoprotein cholesterol (LDL–C)
- Non-high-density lipoprotein cholesterol (non-HDL–C)
- Apolipoprotein A–1 (apoA–1)
- Apolipoprotein B (apoB)
- Apolipoprotein B/apolipoprotein A–1 (apoB/apoA–1)

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Evidence Review

The foundation of the systematic evidence review performed in support of the guideline development process was a series of critical questions related to cardiovascular disease (CVD) risk and prevention in youth. The questions encompassed defined risk factors, predefined outcome measures for each risk factor, and, most importantly, measures of CVD and target organ damage (TOD). Each of these elements was developed and refined through a review of the existing evidence by the Expert Panel. Additional information on the Critical Questions can be found in Table A-1 in Appendix A of the original guideline document.

To inform the identification of studies related to the critical questions, the Expert Panel held an inservice training with the contractor staff members who would be involved in overseeing the literature review to initiate the evidence review process. In addition, a series of group training sessions was held with the contractor staff at appropriate points throughout the process to clarify the scope of the review and expectations for supporting the production of high-quality, evidence-based guidelines.

Search Parameters

Based on the critical questions, risk factors, and types of CVD TOD of interest, search parameters were developed to identify published studies relevant to pediatric cardiovascular (CV) risk reduction. This process involved determining appropriate databases, dates, terms, and limits for the search, as described below.

Databases

Searches were performed in the following databases:

- PubMed/MEDLINE
- Cochrane Database of Systematic Reviews
- National Guideline Clearinghouse (NGC)

Searches were first conducted in PubMed/MEDLINE. Only unique studies from subsequent searches in the Cochrane database and NGC were retained for consideration (i.e., those studies that were not already captured in the initial PubMed/MEDLINE search).

In addition to these databases, a preliminary search of EMBASE was conducted. The great majority of studies identified in this preliminary search were also found in the other databases; therefore, it was determined that proceeding with a complete EMBASE search would not contribute significant additional information to the review.

The literature search allowed for further input by the Expert Panel to ensure that in-scope studies were not overlooked. Members of the Expert

Panel contributed additional relevant studies based on their routine scanning of the literature. A supplementary literature search was also conducted to identify potentially relevant studies authored by members of the Expert Panel. Additional studies identified by these supplementary methods were included only if they met the same criteria for inclusion established for the primary evidence review.

Search Dates

Original searches in PubMed/MEDLINE, Cochrane, and NGC captured studies published between January 1, 1985, and December 31, 2006. Recognizing the timelag inherent in screening a large body of literature and developing evidence tables, the Expert Panel then called for an update of these searches to be conducted for the period between January 1, 2007, and June 30, 2007.

The Expert Panel established June 30, 2007, as the closing publication date for literature to be entered into the evidence review for these Guidelines. The Expert Panel recognized that, given the scope of these Guidelines and the nature of ongoing research in relevant areas, research findings might appear thereafter with the potential to have a material impact on one or more recommendations in the Guidelines. Therefore, to optimize the currency of the Guidelines, the Expert Panel sought, prospectively, to enable consideration of directly relevant, significant peer-reviewed evidence that might appear after the closing date. During a conference call convened on January 21, 2008, the Expert Panel Science Team established the following criteria to guide the full Expert Panel's consideration of studies published after the closing date:

- Any peer-reviewed published study identified by a member of the Expert Panel, as part of his or her routine surveillance of the literature, that is directly relevant to the recommendations of the Expert Panel will be considered for inclusion.
- To be included by the Expert Panel as evidence, the corresponding Risk Factor Team, or the full Expert Panel if applicable at a broader level, must judge that the findings of such recently published studies have the potential for a material impact on the content or strength of the recommendations of the Expert Panel.
- Such studies must meet the same basic criteria for inclusion established for the primary evidence review.
- If there is a difference of opinion about inclusion of a study, a final decision will be made by the Expert Panel Chair.
- Studies that are selected for inclusion will undergo abstraction and full text review by the process established for the primary evidence review. To distinguish it from the body of evidence assembled via the systematic literature search conducted through the closing date of June 30, 2007, the body of evidence from any such more recent studies will be documented separately from the evidence tables comprising data from the original search.

Search Terms

To explore the most appropriate search strategy and examine the sensitivity and specificity of particular search terms, an initial search was done in PubMed/MEDLINE. This search used broad medical subject heading (MeSH) terms and text words for the concepts of pediatric/young adult populations, CVD/TOD, and the risk factors. Terms were combined using the Boolean operators "AND," "OR," and "NOT," which are described briefly in Table A–3 in Appendix A of the original guideline document.

The preliminary, broad search of PubMed/MEDLINE identified in excess of 1 million citations, signaling the need to refine the search terms to identify the most relevant ones. In consultation with the Expert Panel, key refinements in the search strategy were made, including (1) the use of major MeSH terms rather than MeSH terms, where appropriate; (2) the use of title and abstract terms rather than text words; (3) a reduction of the number of terms for each concept, leaving only the most central and essential terms; and (4) the application of excluded concepts to the search (in the form of "NOT" terms).

In the final search strategy, a combination of MeSH terms, major MeSH terms, and title and abstract terms was employed to identify the full range of relevant literature. Search terms were identified to capture studies in the pediatric and young adult target populations (ages 0–21 years) that also addressed CVD/TOD and/or at least one of the risk factors. Specific search terms are provided in Table A–9 in Appendix A of the original guideline document.

Search Limits

A set of limits was applied to the search to help refine the results to the most useful types of studies. The first level of basic search limits included:

- *Publication date*: published between January 1, 1985, and June 30, 2007
- *Language*: English language abstract or full text
- *Publication type*: no editorials, letters, comments, case reports, or non-systematic reviews

Search terms and field tags used to apply these limits to the search are provided in Table A–9 in Appendix A of the original guideline document.

In addition to these basic limits, search terms were used to exclude studies examining certain out-of-scope conditions. For example, during a preliminary review of the literature, many studies were identified that focused on various pediatric conditions such as Kawasaki disease, otitis

media, or congenital heart diagnoses. Through consultation with the Expert Panel, search terms were developed for the most commonly observed out-of-scope conditions. Studies containing these terms were prospectively excluded by using the Boolean operator "NOT."

Search Results

Systematic Reviews, Meta-Analyses, Randomized Controlled Trials, and the Guidelines

After applying the initial limits and using terms to eliminate out-of-scope concepts, the number of results returned from the original literature searches was still in excess of 60,000 citations. Given the size of these literature results, the Expert Panel determined that part of the review would focus on certain study types that would be most useful to the Expert Panel during Guidelines development: systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), and guidelines. Search terms and field tags identifying study type were used to select these studies in the PubMed/MEDLINE database.

Secondary studies, such as SRs and MAs, compile results from primary analyses and, in some cases, review of these study types may lessen the need to examine primary evidence on a topic. However, given the breadth of this evidence review, there were no instances in which an SR or MA captured the entire scope of interest of a critical question; therefore, this review depended on RCTs as an important source of primary data on relevant interventions.

The schematic in Figure A–1 in Appendix A of the original guideline document presents a simplified, high-level depiction of how the key search concepts were combined to achieve the overall search strategy.

In childhood, much of the evidence linking risk factors to atherosclerosis comes from epidemiologic studies. Therefore, in addition to including SRs, MAs, RCTs, and guidelines in the review, the Expert Panel determined that it was necessary for the evidence review to include major epidemiologic studies selected by the Expert Panel. These studies represent landmark longitudinal and natural history studies and other sentinel work that have provided important information and insight about atherosclerosis and CV risk in children. The major observational studies that were included are listed in Table A–4 in Appendix A of the original guideline document.

A separate targeted search of PubMed/MEDLINE was conducted to identify literature relevant to these major studies related to the risk factors for the inclusive period of the evidence review from January 1, 1985, to June 30, 2007. The observational literature was also updated by the Expert Panel using the same criteria developed for the classic evidence review. Terms used to conduct this search are provided in Table A–10 in Appendix A of the original guideline document. National Heart, Lung and Blood Institute (NHLBI) staff reviewed the titles and then the abstracts for studies to be included based on the 14 risk factors under review. When a longitudinal study reported results of the same variables at increasing intervals from the beginning of the observational period, the most recent report detailing the longest period of observation was selected for inclusion. Duplicate reports of the same results were excluded. The observational studies to be included in the evidence review were selected by the Expert Panel Risk Factor Teams.

Additional References

In an evidence-based review, studies included are generally limited to RCTs, SRs, and MAs. In addition to the epidemiologic studies described above, Expert Panel members also included studies that provided important information for each risk factor, defining the context in which the Guidelines' recommendations were developed. These references are not part of the evidence tables but are identified sequentially throughout the text and will be listed in Appendix B of the original guideline document by section in numeric order, as identified in the text. Of particular importance were studies of genetic conditions impacting CV risk status and natural history studies of specific diseases known to be associated with accelerated atherogenesis.

Inclusion and Exclusion Criteria

In preparation for review of the literature, inclusion and exclusion criteria were developed by the Expert Panel. These criteria outlined additional boundaries for the review. Certain criteria were applied only by the Expert Panel, given that judgments regarding the application of these criteria required relevant clinical expertise.

Inclusion Criteria

- Pertained to at least one of the specified risk factors and measured at least one of the predetermined outcomes
- Related to at least one of the critical questions
- Focused on the target population (ages 0–21 years)
    - For longitudinal studies and other studies with extended followup periods, the population was required to be in this age range at initiation, and this subcohort could be identified in subsequent analyses.
    - For the Guidelines, the target population was required to include at least part of this age range.

- Conducted in Europe, North America, Australia, New Zealand, Japan, or Israel
- In 2004, an NHLBI-appointed Task Force published *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*. This report included a complete review of the current evidence on this subject and detailed recommendations for managing blood pressure (BP) throughout childhood. These recommendations were used as the basic recommendations for BP management for these Guidelines and are considered complete until 2003 when the review for the report ended. The literature review for BP, therefore, was limited to January 1, 2003, through June 30, 2007; selected studies from 2008 identified by the Expert Panel that met all the criteria for inclusion in the evidence review were also included.

Exclusion Criteria

- Any study not meeting the above requirements was excluded from the review.
- Studies that otherwise met inclusion criteria but that were found, upon examination, to have measured risk factors in only an incidental way or as part of assessing the safety of an intervention were excluded. For example, a study of an asthma medication might measure BP to ensure that there were no adverse effects of the medication. Such studies that measured in-scope outcomes that were not linked to a risk factor condition were excluded from the review.
- Duplicate reports of findings based on the same original studies were generally excluded. For instances in which a series of studies (typically longitudinal studies or large RCTs) reported results for the same outcome measures over a period of time, the most recent studies and main results of trials were typically retained and older studies were excluded. These determinations were made individually during the review of each study.
- Studies that did not meet basic internal/external validity standards (e.g., as a result of narrowly defined patient population) were excluded.
- Studies that addressed the target population, often as part of a broader age range, but did not provide findings specific to patients in the target age range were excluded.
- Studies were excluded that on closer inspection were found not to be SRs, MAs, RCTs, guidelines, or reports from the selected epidemiologic studies.
- Studies were excluded that had an insufficient number of patients at followup to draw meaningful conclusions.
- Studies conducted in patients with diabetes focused on interventions that were related exclusively to glycemic control were excluded.
- For studies that focused on smoking as a risk factor, those that reported on interventions related to policymaking or merchant behavior were excluded.

During the review process, inclusion and exclusion criteria were modified to account for topics identified as irrelevant and certain included topics were clarified. Throughout this process, abstractors and the Expert Panel were in close contact to resolve questions regarding the application of inclusion/exclusion criteria to individual studies.

Literature Review Process

After completing electronic searches in each database, a total of 11,231 SRs, MAs, RCTs, guidelines, and major observational studies were identified for review. The distribution of search results by database and study type is presented in Table A–5 in Appendix A of the original guideline document.

Abstracts and citations for these studies were compiled and organized using Reference Manager.

Figure A–2 in Appendix A of the original guideline outlines the phases of the literature review process and the number of studies excluded at each stage. Throughout each review phase the Expert Panel provided guidance regarding the appropriate application of inclusion and exclusion criteria.

Following the review of titles and abstracts, trained abstractors conducted a full-text review of the studies and excluded additional studies. NHLBI staff also reviewed the full text of these studies and identified additional studies to exclude. Following the full-text review phase, an additional 200 studies were excluded. Citations for studies excluded at the full-text level are provided online, along with the complete evidence tables.

In addition to a review of the studies captured through the literature search process (i.e., studies published between January 1, 1985, and June 30, 2007), the NHLBI and the Expert Panel identified an additional 29 relevant studies that were published after June 30, 2007, for inclusion in the review.

Number of Source Documents

At the end of the review process, a total of 664 studies were included for review—including 51 systematic reviews, 34 meta-analyses, 304 randomized controlled trials, 84 guidelines, and 191 observational studies.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Quality for Grades of Evidence

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the Guidelines' target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Collection and Quality Control

Systematic Reviews, Meta-Analyses, Randomized Controlled Trials, and Guidelines

To capture information from in-scope studies, Excel tables were developed and used for data abstraction of each study type (i.e., systematic review [SR], meta-analysis [MA], randomized controlled trial [RCT]). Through discussion the Expert Panel, the types of information collected and the format of the tables were refined. Data collected in the abstraction tables included basic information about the study (e.g., year of publication), objective, patient population, intervention and comparator/control (if applicable), outcomes measured, and results. Data abstracted varied by study type. A complete list of data fields and definitions for these fields is provided through the National Heart, Lung and Blood Institute (NHLBI) Web site.

To complete the data abstraction tables, trained abstractors reviewed full-text versions of each in-scope study. Two reviewers examined each full-text study; the first reviewer abstracted the appropriate data from each study, while the second reviewer concentrated on ensuring the accuracy and quality of data entered by the first reviewer as part of a thorough quality control process. For RCTs, contractor staff abstracted information for specific columns, including basic information about the study, objective, patient population, intervention and comparator/control (if applicable), and outcomes measured. For SRs and MAs, the contractor staff abstracted information for all columns. For observational studies, contractor staff abstracted the basic informational data, but full-text review and data entry were performed by NHLBI staff.

After data abstraction by the contractor, the data abstraction tables were submitted to the NHLBI and the Expert Panel for review and/or completion of abstraction. For all study types, Expert Panel members were responsible for verifying data entered by the contractor. For RCTs, Expert Panel members and NHLBI staff selected the outcome variables to be abstracted and entered the results in the evidence tables, as well as recorded study results and conclusions. To facilitate this process, studies were forwarded to the relevant subcommittee within the Expert Panel, according to the primary risk factor of focus. For example, a study that examined the use of an intervention to improve cholesterol levels would have been forwarded to the subcommittee on lipids. Study reviews were rotated to ensure that each was reviewed by two subcommittee members. Subcommittee members completed abstraction of established columns and, in several cases, requested the addition of extra columns in the evidence tables to capture more specific information pertaining to the risk factor of interest. When Expert Panel members were not in agreement regarding such matters as study relevance or abstraction of specific data, these matters were brought to the Expert Panel Chair for resolution.

In addition to basic information about study design and results, aspects of study quality were considered by the Expert Panel during data abstraction. A customized quality grading system was developed to support the Expert Panel's interpretation of individual studies, particularly with regard to methodology and study design considerations. This novel grading system, the development of which drew largely from several existing grading schemes, was incorporated into the electronic data abstraction tables. The system used an algorithm that generated a quality grade for individual RCTs, according to the criteria outlined in Tables 11 and 12 in Appendix A of the original guideline document. SRs, MAs, and observational studies did not receive an individual quality grade.

After completion of data abstraction, evidence tables displaying key study information were developed from the data abstraction tables using Excel for use by the Expert Panel. These standard evidence tables were then sorted in a customized way for each subcommittee, so as to best support the Guidelines development process. Final evidence tables for all included SRs, MAs, RCTs, and observational studies are provided online at http://www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm.

Although reports of guidelines were captured as part of the literature search, they were not incorporated into evidence tables. Instead, the guidelines were reviewed for relevance, and those that were in scope were categorized according to the risk factor(s) addressed. A list of the in-scope guidelines was made available to Expert Panel members for their reference; full-text versions were made available as needed. Citations for in-scope guidelines, by risk factor, are also provided online.

Major Observational Studies

Excel tables were also developed for the epidemiologic observational studies, with basic information about each study entered into tables by skilled abstractors from contractor staff. Full-text review and abstraction of each study were performed by NHLBI staff, including identification of outcome variables and review of results and conclusions. These tables were then reviewed by Expert Panel members, who selected 191 studies as relevant to the evidence review. The tables were primarily categorized by risk factor and then sorted using the terms developed by the relevant Risk Factor Teams for inclusion in the review. Expert Panel members added additional relevant reports from any of these observational studies that appeared after conclusion of the formal review. The evidence tables for the observational studies are also included on the NHLBI Web site.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Expert Panel and Subcommittee Discussion

Following establishment of the Expert Panel, in-person meetings were held in October 2006, February 2007, June 2008, and October 2008. These meetings enabled Expert Panel members to discuss key elements of the systematic evidence review, consider the approach and scope of the Guidelines, and review and refine the Guidelines' recommendations.

To facilitate discussion of the evidence related to particular risk factors, multiple subcommittee conference calls were held from February to December 2008, along with a continuous electronic correspondence. Across the seven subcommittees, more than 500 conference calls were completed. During these calls, subcommittee members established processes for developing and finalizing the Guidelines' recommendations for each risk factor and progressively shaped the final recommendations in the Guidelines. A SharePoint Web site was created to enable subcommittee members to share draft recommendations.

Established Parameters for Guidelines Recommendation Development

The Expert Panel adopted an evidence grading system from the American Academy of Pediatrics (AAP) to assess the quality of the body of evidence as a whole and the evidence in support of particular statements. The grading system is shown in the "Rating Scheme for the Strength of the Evidence" field; it was modified by the addition of genetic natural history studies to the grade B evidence category; an example of a genetic natural history study is the development of atherosclerosis in a child with homozygous familial hypercholesterolemia who has severely elevated cholesterol levels from birth. Studies of such genetic conditions are believed to represent a natural intervention and to function as surrogates for a specific lifelong risk exposure. Genetic variation shares features with random assignment in clinical trials in that the variation occurs by chance within a society and the presence of the genetic variation does not alter exposure to environmental or other factors. Drawing from the same AAP system, the "Rating Scheme for the Strength of the Recommendations" field depicts the Guidelines' definitions for evidence-based statements.

The Expert Panel also developed a definition of consensus to guide decision making regarding Guidelines recommendations within the

subcommittees and among the full Expert Panel. The final definition included the following elements:

- Committee deliberations regarding a given recommendation generally reflected deference to the expert risk factor subcommittee that was originally charged with critically appraising the evidence and drafting the recommendation.
- Voting was "in support of" or "opposed to" a recommendation.
- Agreement by at least 80 percent (or 11 of 14 members) of the Expert Panel constituted a strong consensus. A recommendation with this level of agreement is presented in the Guidelines as a consensus of the Expert Panel. However, discussion of the issues in the Guidelines document may address areas of difference.
- A proposed recommendation that was supported by less than 60 percent (or less than 8 of 14 members) of the Expert Panel was not included in the Guidelines. However, review of the subject could be included in the discussion for that risk factor area.
- Agreement by 60–80 percent (9 or 10 of 14 members) of the Expert Panel constituted a moderate consensus in support of the recommendation. A recommendation with this level of agreement was presented with that language in the Guidelines and accompanied by discussion of the conflicting issues. In developing the discussion in support of a recommendation, the actual vote of the Expert Panel was considered.

In considering the various pediatric age groups covered by the Guidelines' recommendations, the Expert Panel agreed to formulate the Guidelines' recommendations according to the chronological timetable used by the AAP *Bright Futures* program:

- Preconception/prenatal
- 0–12 months
- 1–4 years
- 5–10 years
- 11–17 years
- 18–21 years

Studies were not always specific to an age group, and the Expert Panel used judgment in determining how those studies informed age-specific recommendations.

Completion of the Guidelines

At the final full Expert Panel meeting in October 2008, the Expert Panel reviewed each recommendation proposed by each subcommittee in detail. According to the established definition of consensus, the Expert Panel agreed on a complete set of recommendations and supporting text in the draft Guidelines report.

Rating Scheme for the Strength of the Recommendations

Guidelines' Definitions for Evidence-Based Statements

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent (Grade A or B). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade C or D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel believes that the benefits exceed the harms but the quality of the evidence is not as strong (Grade B or C). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should generally follow a recommendation but remain alert to new information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and

Statement Type	Definition	Implication
		family preferences should have a substantial influencing role.
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and should be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preferences should have a substantial influencing role.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

In April 2009, a draft version of the Guidelines was circulated to other National Institutes of Health (NIH) Agencies and multiple professional organizations for review and comment. The draft version was also posted on the National Heart, Lung and Blood Institute (NHLBI) Web site for public comment for a 30-day period from June 19 to July 20, 2009. In total, the Expert Panel considered more than 1,000 comments from more than 50 reviewers, and individual responses were developed for more than 1,000 comments. The draft version of the Guidelines also underwent a separate review by the NHLBI and the U.S. Department of Health and Human Services (HHS). After considering all comments, consistent with applicable Federal requirements, the Expert Panel made appropriate revisions to the draft report. The summary report was published in final form November 11, 2011.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The promotion of cardiovascular (CV) health and the identification and management of specific risk factors from infancy into young adult life
- The evidence review supports the concept that early identification and control of dyslipidemia throughout youth and into adulthood will substantially reduce clinical cardiovascular disease risk beginning in young adult life. Preliminary evidence in children with heterozygous familial hypercholesterolemia (FH) with markedly elevated low-density lipoprotein-cholesterol (LDL–C) indicates that earlier treatment is associated with reduced subclinical evidence of atherosclerosis.

Potential Harms

Statins

- Adverse effects from statins are rare at standard doses but include myopathy and hepatic enzyme elevation. Asymptomatic hepatic enzyme elevation is fairly common in adults on statin therapy but is reversible with medication change and is not clearly associated with increased risk of liver disease. Myopathy—muscle pain and weakness with creatine kinase elevations more than 10 times the upper limits of normal range— typically occurs in fewer than 1 in 10,000 adult patients. Rhabdomyolysis, a very rare occurrence in adults on statin therapy reported at 3 per 100,000 person-years, did not occur in any of the pediatric trials but the total number of subjects is too small to evaluate that risk. The risk of rhabdomyolysis increases with use of higher doses and interacting drugs. Drug interactions with statins occur primarily with drugs that are metabolized by the cytochrome P–450 system, the primary mode of metabolism for the majority of statins. Drugs that potentially interact with statins include fibrates, azol antifungals, macrolide antibiotics, antiarrhthymics, and protease inhibitors. When statin use is initiated, prescribing information must be routinely consulted for potential drug interactions. Patients need to be cautioned about potential future medication interactions, and pediatric care providers need to assess this whenever any new medication is introduced.
- Females taking a statin should be counseled about risks associated with pregnancy and appropriate contraception strategies if indicated.

Bile Acid Sequestrants

The bile acid sequestrants commonly have gastrointestinal side effects (gas, bloating, constipation, cramps), and these significantly affect compliance. Since the bile acid sequestrants reduce bile salts, which are important for intestinal lipid absorption, there has been some concern regarding malabsorption of fat-soluble vitamins (A, D, E), and routine supplementation with a daily multivitamin and folate may be indicated. Also, bile acid sequestrants may interfere with the absorption of some medications; this potential interaction should be specifically evaluated whenever any additional medication is needed.

Refer to Table 9–10 in the original guideline document for adverse effects of other medications used to treat hyperlipidemia.

Contraindications

Contraindications

- Statins are contraindicated in pregnancy.
- Hydroxy-3-methyl-glutaryl coenzyme A (HMG CoA) reductase inhibitors may be contraindicated with potentially interactive medications (cyclosporine, niacin, fibric acid derivatives, erythromycin, azole antifungals, nefazodone, and many human immunodeficiency virus (HIV) protease inhibitors.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Lipids and lipoproteins. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. p. 184-281. [158 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

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Guideline Developer(s)

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Guideline Committee

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents

Composition of Group That Authored the Guideline

Expert Panel Members: Stephen R. Daniels, M.D., Ph.D. (*Panel Chair*), Professor and Chairman, Department of Pediatrics, University of Colorado School of Medicine, Pediatrician in Chief and L. Joseph Butterfield Chair of Pediatrics, The Children's Hospital; Irwin Benuck, M.D., Ph.D., Northwestern University Feinberg School of Medicine, Chicago, IL; Dimitri A. Christakis, M.D., M.P.H., Director, Child Health Institute, Associate Professor of Pediatrics, University of Washington; Barbara A. Dennison, M.D., Director, Policy and Research Translation Unit, Division of Chronic Disease and Injury Prevention, New York State Department of Health; Samuel S. Gidding, M.D., Chief, Division of Pediatric

Cardiology, Department of Pediatrics, Nemours/Alfred I. duPont Hospital for Children; Matthew W. Gillman, M.D., M.S., Department of Ambulatory Care and Prevention, Harvard Pilgrim Health Care; Mary Margaret Gottesman, Ph.D., R.N., CPNP, Cochairperson, Bright Futures Pediatric Implementation Project, Ohio State University College of Nursing; Peter O. Kwiterovich, M.D., Professor of Pediatrics and Medicine, Lipid Research Unit; Patrick E. McBride, M.D., M.P.H., Professor of Medicine and Family Medicine, Codirector, Preventive Cardiology Program, University of Wisconsin School of Medicine and Public Health; Brian W. McCrindle, M.D., M.P.H., Cardiologist, Division of Cardiology, Department of Pediatrics, Section Head, Clinical Epidemiology, The Hospital for Sick Children; Albert P. Rocchini, M.D., Professor of Pediatrics, Division Chief, Cardiology, C.S. Mott Children's Hospital; Elaine M. Urbina, M.D., Preventive Cardiology Program, Cincinnati Children's Hospital Medical Center; Linda V. Van Horn, Ph.D., R.D., Professor of Preventive Medicine, Feinberg School of Medicine, Northwestern University; Reginald L. Washington, M.D., Chief Medical Officer, Rocky Mountain Hospital for Children

Refer to the original guideline document for members of the National Heart, Lung, and Blood Institute staff and for names of the contractor support.

Financial Disclosures/Conflicts of Interest

Expert panel members disclosed relevant financial interests to each other prior to discussions. The following financial interests are reported in the publication in the J*ournal of Pediatrics*:

Dr. Benuck, Dr. Christakis, Dr. Dennison, Dr. O'Donnell, Dr. Rocchini, and Dr. Washington have declared no relevant relationships.

Dr. Daniels has served as a consultant for Abbott Laboratories and Merck, Schering-Plough. He has received funding/grant support for research from the NIH.

Dr. Gidding has served as a consultant for Merck, Schering-Plough. He has received funding/grant support for research from GlaxoSmithKline.

Dr. Gillman has given invited talks for Nestle Nutrition Institute and Danone. He has received funding/grant support for research from Mead Johnson, Sanofi-aventis and the NIH.

Dr. Gottesman has served on the Health Advisory Board, Child Development Council of Franklin County. She was a consultant to Early Head Start for Region 5B. She has written for iVillage and taught classes through Garrison Associates for the State of Ohio, Bureau of Early Intervention Services and Help Me Grow program. She has received funding/grant support for research from NIH.

Dr. Kwiterovich has served as a consultant or advisory board member for Merck, Schering-Plough, Pfizer, Sankyo, LipoScience and AstraZeneca. He has served on speaker bureaus for Merck, Schering-Plough, Pfizer, Sankyo, Kos and AstraZeneca. He has received funding/grant support for research from Pfizer, Merck, GlaxoSmithKline, Sankyo and Schering-Plough.

Dr. McBride has served as a consultant or advisory board member for Bristol-Myers Squibb, and Merck. He has served on speakers bureaus for Kos, Merck and Pfizer. He declared no relevant relationships since July 2007.

Dr. McCrindle has been a consultant for Abbott, Bristol-Myers Squibb, Daichii Sankyo and Roche. He owns stock in CellAegis. He reports funding/grant support for research from AstraZeneca, Sankyo, Merck, Schering-Plough and the NIH.

Dr. Urbina reports funding/grant support for research from Merck, Schering-Plough, Sankyo and the NIH.

Dr. Van Horn has provided advice to Chartwells School Food Service. She has received funding/grant support for research from General Mills and the NIH.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Heart, Lung, and Blood Institute (NHLBI) Web site .

Print copies: Available from the NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: nhlbiic@dgsys.com.

Availability of Companion Documents

The following are available:

- Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Summary report 2011. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. 125 p. Electronic copies: Available in Portable Document Format (PDF) from the National Heart, Lung, and Blood Institute Web site .
- Evidence tables. Electronic copies: Available in PDF from the National Heart, Lung, and Blood Institute Web site .

Patient Resources

Various resources for the public about heart and vascular diseases are available from the National Heart, Lung and Blood Institute Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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